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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/647,654

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Philip W. Ingham

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ROPES & GRAY LLP

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EXAMINER

MACFARLANE, STACEY NEE

ART UNIT

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1649

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/647,654	Applicant(s) INGHAM ET AL.	
	Examiner STACEY MACFARLANE	Art Unit 1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 October 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,5,6,11-13,23-26 and 49-81 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,5,6,11-13,23-26 and 49-81 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>5/22/2008</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Amendment

1. Claims 1, 2, 6, 23, 25, 26, 49, 50, 52, 53, 63, 64, 66-75 and 77-81 have been amended as requested in the amendment filed on October 6, 2008. Following the amendment, claims 1-3, 5, 6, 11-13, 23-26 and 49-81, in so far as they read upon SEQ ID NO: 13, are pending and are under examination in the instant office action.
2. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.
3. Applicant's arguments filed on October 6, 2008 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Priority

4. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged but is found to not be in compliance with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120, 121, or 365(c) as follows: Claims 1-3, 5, 6, 11-13, 23-26 and 49-81 will be given the effective filing date of December 14, 1994, for reasons of record in the Office action mailed June 3, 2008.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

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art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-3, 5, 6, 11-13, 23-26 and 49-81 stand as rejected under 35 U.S.C. 112, first paragraph, for reasons of record in the Office action mailed June 3, 2008. The specification, while being enabling for methods of promoting growth, differentiation and/or survival of embryonic neural tube or neural plate cells by administering a Shh polypeptide consisting of SEQ ID NO: 13 or the N-terminal proteolytic fragment thereof (as defined by line 25, page 4 of the specification), does not reasonably provide enablement for methods comprising administration of any other means for binding a naturally occurring hedgehog receptor as disclosed. Thus, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

On pages 14-15 of Remarks filed October 6, 2008, Applicant traverses the rejection on the grounds that, "Examiner's analysis of the Wands factors provides no indication of whether and how the Examiner has weighed the extensive post-filing evidence provided to support the enablement of the claimed subject matter. Rather, the review of the Wands factors provided on pages 11-15 of the Office Action offers nothing more than conclusory statements unsupported by objective evidence and without an assessment of how the evidence and arguments provided by Applicants' were balanced or considered" and that Applicants respectfully submit that the Examiner has not satisfied the burden necessary for a rejection of enablement in the face of the teachings of the specification and objective evidence provided by Applicants. While this

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argument and the post-filing support have been reviewed in full they are not found persuasive to overcome the rejection for the following reasons.

In order to satisfy the enablement requirement of section 112, an applicant must describe the manner of using the invention “in such full, clear, concise and exact terms as to enable any person skilled in the art ... to make and use the same...” 35 U.S.C §112, paragraph 1. Thus, the invention must be enabled at the time of filing and, therefore, the enablement requirement cannot be supported by later obtained experimental results. *In re Rasmusson*, the Court held that

“If mere plausibility were the test for enablement under section 112, applicants could obtain patent rights to “inventions” consisting of little more than respectable guesses as to the likelihood of their success. When one of the guesses later proved true, the “inventor” would be rewarded the spoils instead of the party who demonstrated that the method actually worked. That scenario is not consistent with the statutory requirement that the inventor enable an invention rather than merely proposing an unproved hypothesis”. *In re Rasmusson v. SmithKline Beecham Corp.* 75 USPQ2D 1297, p1301.

Therefore, the application must have enabling support therein or evidence must be provided demonstrating that one of ordinary skill in the art would have been able to make and use the invention with a reasonable expectation of success with techniques that were well-known in the art at the time of filing.

Claims 1-3, 5, 6, 11-13, 23-26 and 49-81 broadly encompass methods comprising contacting a dopaminergic cell, a mammalian neuronal cell or any non-embryonic mammalian cell comprising contacting said cell with SEQ ID NO: 13 or a 19 kDa MW, N-terminal fragment thereof. Claims 66-81 are drawn to the method comprising contacting cells with any means for binding a naturally occurring hedgehog

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receptor disclosed within the specification. Paragraph [0074] discloses that nucleic acids encoding vertebrate hedgehog proteins, the hedgehog proteins themselves, antibodies immunoreactive with hedgehog proteins, and agents, identified by screening methods, are all encompasses as means for binding a hedgehog receptor. The sole evidence presented within the disclosure is with respect to the method as performed in embryonic neural tube cells and comprising contacting said cells with SEQ ID NO: 13 or a 19 kDa MW, N-terminal fragment thereof. The instant specification provides neither enough guidance for such method of determination, nor working examples, which would show that the claimed method was successfully achieved with any other non-embryonic cell type (for example, the method as performed in vivo in adult mammals) or by any other means for binding a receptor as disclosed within the specification. Absent such guidance, one of ordinary skill in the art would rely solely on that which was known in the art at the time of filing.

While the skill level in the art is high, the level of predictability with respect to the claimed method is low. The state of the art at the time of filing recognized that the hedgehog family of polypeptides induces the differentiation of the ZPA, notochord and floor plate, which are essential stages along the pathway of embryonic motoneuron and neuronal phenotypes. Since the cells of these regions give rise to all neurons, then the induction of a dopaminergic neuronal fate is induced by hedgehog as well and Applicant's data demonstrating that, upon contact with hedgehog, embryonic cells of from these regions are induced to proliferate, differentiate and/or survive, confirms this state of the art. Applicant, however, has not demonstrated that contact with hedgehog,

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an N-terminal portion thereof, or a "means for" hedgehog signaling induces the proliferation, differentiation, or survival of any cell, as broadly claimed. Therefore, Examiner maintains, for reasons made of record, that given the breadth of the claims, the deficiency of guidance within the instant disclosure, and a lack of guidance within the art at the time of filing, one of ordinary skill in the art would require undue experimentation to discover how to practice Applicant's invention to the full scope as claimed. Such experimentation goes beyond the realm of what would be considered within the art as routine experimentation, and constitutes undue experimentation on the part of the practitioner. Therefore, the claims are rejected for lack of enabling support.

Conclusion

7. No claim is allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STACEY MACFARLANE whose telephone number is (571)270-3057. The examiner can normally be reached on M-W and ALT F 5:30 to 3:30, TELEWORK-Thursdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane
Examiner
Art Unit 1649

/John D. Ulm/
Primary Examiner, Art Unit 1649

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